UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/347,311	07/02/99	PLAETINCK G	B0192/7010

HM12/0621

JOHN R VAN AMSTERDAM
C/O WOLF GREENFIELD & SACKS P C
FEDERAL RESERVE PLAZA
600 ATLANTIC AVENUE
BOSTON MA 02210-2211

EXAMINER	
PENN, M	
ART UNIT	**PAPER NUMBER**
1633	12

DATE MAILED: 06/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/347,311	Applicant(s) PLAETINCK ET AL.	
	Examiner Michael G. Penn	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-91* is/are pending in the application.

4a) Of the above claim(s) *16,22,25-37,46 and 49-91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17-21,23,24,38-45 and 49-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michael G. Penn, Art Unit 1633.

Claims 1-15, 17-21, 23, 24, 38-45, and 47-48 are pending and under consideration in the instant office action.

Election/Restrictions

Claims 16, 22, 25-37, 46, and 49-91 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election to group I-B was made **without** traverse in Paper No. 17.

Specification

The abstract of the disclosure is objected to because it contains legal phraseology in the wording. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

Claims 1-15, 17-21, 23, 24, 38-45, and 47-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of plasmid vectors that initiate transcription of double stranded RNA introduced into *C. elegans*, does not reasonably provide enablement for the use of all vector systems, or the *in vivo*

use of the methods in all organisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The pending application is drawn to methods of *in vivo* gene transfer. While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings available in the art. Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and

discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

With respect to the field of RNA interference, Fire et al. (Fire et al., Nature, Feb. 1998, pp. 806-11) can be viewed as the state of the art at the time of filing. Fire teaches that injection of double stranded RNA results in greatly enhanced interference as compared to single stranded RNA, but that the mechanisms of this interference are unknown (p. 808, 1st col., 2nd paragraph; p. 809, 2nd col., 3rd paragraph). Because the mechanisms of the RNA interference at the time of filing were unknown, the technology of RNA interference by double stranded RNA can be viewed as being highly unpredictable.

The specification of the instant application describes methods of using a plasmid to deliver DNA that is capable of initiating transcription of double stranded RNA. No working examples or enabling data is provided using any other vector system, thus the scope must be narrowed to only plasmid vector systems. Viral vector systems can affect transcription of genes at the cellular level, with viral genes specifically affecting or interfering with transcription and translation. For example, the adenovirus early genes

activate and enhance cellular promoters and can also interact with cellular oncogenes. Because the mechanism of RNA interference is unknown, and no data with vector systems other than plasmid vectors has been provided, at best, the pending application is enabled for only the use of plasmid vector systems. Moreover, a high level of skill is required to generate cDNA libraries, and one skilled in the art at the time of filing would need more guidance than that provided in the specification in order to generate libraries of any cell type, from any or all species. For example, in some instances it will be desirable to use plasmid DNA vectors for cDNA library generation, whereas in other instances bacteriophage vectors will be used to facilitate library generation, with a multitude of different bacteriophage vectors suited to particular circumstances. Furthermore, the specification only describes delivery of the plasmid to *C. elegans* and no other organisms (e.g. mammals). Because the mechanism of RNA interference is unknown and no data with organisms other than *C. elegans* is provided, the pending application is enabled only for the use of the methods in *C. elegans*.

Therefore, considering the unpredictability of the art of in vivo gene delivery, the limited guidance provided in the specification, the broad scope of the claims, the limited scope of working examples and lack of enabling data, it would have required one of skill in the art at the time of filing undue experimentation to make and/or use the claimed invention.

Claims 3-15, 17-21, 23, and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-15, 17-21, 23, and 24, as best understood, are readable on a genus of DNA homologs and fragments of DNA homologue(s), wherein none of the identifiers or molecules are claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods containing unspecified molecular structures of molecules that are essential for the making the genus DNA homologs and fragments of DNA homologs as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of DNA homologs and fragments of DNA homologs that must exhibit the disclosed biological functions as contemplated by the as-filed specification.

It is not sufficient to support the present claimed invention directed to a DNA homologs or a fragment of a DNA homolog, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any and/or all other DNA

homologs or fragments of DNA homologs having the biological functions as contemplated by the specification and the claims. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Claiming unspecified molecular structures of DNA homologs or fragments of DNA homologs that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of the claimed DNA homologs or fragments of DNA homologs that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 3-15, 17-21, 23, and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Since the claimed invention is not supported by a sufficient written description for possessing the genus of DNA homologs or a "fragment thereof" as recited in the claims, particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended. Although the specification contemplates using *in silico* techniques to identify DNA homologs, specific guidance as to what homologs or fragments of homologs is not given (p. 14, line 20). A DNA homolog could encompass any number of as yet identified proteins, thus at the time of filing one skilled in the art would not be able to predict what homologs might be used in the invention. Furthermore, a "fragment thereof" could

encompass any number of mutated or truncated forms of the desired DNA homolog, including merely a single nucleotide. Accordingly, because of the unpredictability of the function of these derivatives and the sheer number of possible "fragments thereof," at the time of filing one skilled in the art would not be able to predict that delivery of a vector encoding every possible fragment of the proteins or polypeptides mentioned would function as intended without undue experimentation.

Therefore, considering the unpredictability of the art, the limited guidance provided in the specification, the broad scope of the claims, the limited scope of working examples and lack of enabling data, it would have required one of skill in the art at the time of filing undue experimentation to make and/or use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15, 17-21, 23, 24, 38-45, and 47-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "particular phenotype in a cell," and "isolating a particular phenotype of said cell." The use of the word phenotype renders this claim vague and indefinite. A phenotype is a set of observable characteristics of an organism that can be the result of factors including genotype, environment, and lifestyle, and the interaction between these factors (http://genomics.phrma.org/lexicon/p.html#phenotype; June 4, 2001). A phenotype is not "in a cell," nor can a phenotype "isolated." Moreover,

in claim 1, the word "particular" is unclear, as what limits a "particular" phenotype would define are not definite. Furthermore, the phrase "suitable vector" is vague and indefinite as it is unclear what suitability is desired. Additionally, the phrase "appropriate transcription factor" is vague and indefinite. It is unclear what would be considered appropriate. Clarification is required.

Claim 3(c) recites the phrases "an appropriate vector" and "appropriate transcription factor." It is unclear what would be considered appropriate. For example, is the vector appropriate for gene expression, toxicity, transfection efficiency, or all or none of these? Furthermore, the phrase "suitable promoter" is vague and indefinite as it is unclear what suitability is desired. Clarification is required.

Claim 7, 8, 10, 11 are vague and indefinite for the use of the word "suitable." It is unclear what suitability is desired. Clarification is required.

Claim 12 is vague and indefinite because it is not clear what a "known phenotype" would encompass. Clarification is required.

Claim 13 is vague and indefinite because of the use of the word "suitable." It is unclear what suitability is desired. Claim 13 is further vague and indefinite because of the use of the word "appropriate." It is unclear what would be considered an appropriate transcription factor. Clarification is required.

Claim 14 is vague and indefinite because of the use of the phrase "suitable or further vector." It is unclear what suitability is desired, and additionally it is unclear what a further vector is meant to encompass. Clarification is required.

Claim 38 is vague and indefinite because of the use of the word "appropriate." It is unclear what would be considered and appropriate transcription factor. Clarification is required.

Claims 20 and 48 recite a broad limitation followed by a narrow limitation. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 20 recites the broad recitation "a desired phenotype," and the claim also recites "such as resistance or sensitivity to said compound," which is the narrower statement of the range/limitation. Claim 48 recites the broad recitation "species nematoda," and the claim also recites "preferably *C. elegans*," which is the narrower statement of the range/limitation. Clarification is necessary.

Claims 1-15, 17-21, 23, 24, 38-45, and 47-48 appear to be free of the prior art record, however they are subjected to other rejections and revisions. Therefore, no claims are allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Penn who can normally be reached on Monday through Friday from 8:00 am to 4:30 p.m. at (703) 308-2454.

Questions of formal matters can be directed to the patent analyst, Kimberly Davis, who can normally be reached on Monday through Friday from 9:00 am to 5:30 p.m. at (703) 305-3015.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael G. Penn

Deborah Clark

DEBORAH J. R. CLARK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600